

### **Listing of the Claims**

1. (Currently amended) A composition comprising a ~~pre-graft~~ human skin equivalent, said ~~pre-graft~~ skin equivalent having a surface electrical capacitance of from about 40 to about 240 pF ~~measured as the difference in reading over a 10 second interval~~.
2. (Currently amended) The composition of Claim 1, said human skin equivalent having a surface electrical capacitance of from about 80 to about 120 pF ~~measured as the difference in over a 10 second interval~~.
3. (Currently amended) The composition of Claim 1, wherein the combined content of ceramides 5, 6, and 7 in said ~~pre-graft~~ skin equivalent is from about 20 to about 50% of total ceramide content.
4. (Currently amended) The composition of Claim 1, wherein the content of ceramide 2 in said ~~pre-graft~~ skin equivalent is from about 10 to about 40% of total ceramide content.
5. (Currently amended) The composition of Claim 1, wherein said ~~pre-graft~~ skin equivalent comprises keratinocytes selected from the group consisting of primary keratinocytes and immortalized keratinocytes.
6. (Currently amended) The composition of Claim 5, wherein said immortalized keratinocytes are ~~NHKS Near Diploid Immortalized Keratinocyte~~ cells.
7. (Canceled)
8. (Currently amended) The composition of Claim 1, further comprising keratinocytes derived from ~~two different sources~~ a patient.
- 9-54. (Canceled)

## REMARKS

Claims 1 - 6 and 8 are pending in the present application. The following rejections are at issue and are set forth by number in the order in which they are addressed:

1. Claims 6 and 8 are rejected under 35 U.S.C. §112, second paragraph as indefinite;
2. Claims 1, 2, 5, 6, and 8 are rejected under 35 U.S.C. §112, first paragraph as non-enabled;
3. Claims 1, 2, and 5 are rejected under 35 U.S.C. §102(b) as being anticipated by Goretsky et al., Wound Repair and Regen. 3(4):419-25 (1995);
4. Claims 1 and 5 are rejected under 35 U.S.C. §102(b) as being anticipated by Boyce et al., J. Invest. Dermat. 107(1):82-7 (1996);
5. Claims 1 and 8 are rejected under 35 U.S.C. §103(a) as unpatentable over Boyce et al. in view of Suzuki et al., Transplantation 59:1236-41 (1995); and
6. Claims 1, 3, and 4 are rejected under 35 U.S.C. §103(a) as unpatentable over Boyce et al. in view of Ponec et al., J. Invest. Dermat. 109(3):348-55 (1997).

Claims 1 - 6 and 8 have been amended. Unless otherwise noted, the claims have been cancelled or amended to further Applicant's business interests and the prosecution of the present application in a manner consistent with the PTO's Patent Business Goals (PBG; 65 Fed. Reg. 54603 (September 8, 2000)), and not in acquiescence to the Examiner's arguments and while reserving the right to prosecute the original (or similar) claims in the future. None of the claim amendments made herein are intended to narrow the scope of any of the amended claims within the meaning of *Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co.*, 234 F.3d 558, 56 USPQ2d 1865 (Fed. Cir. 2000) or related cases. The amendments find more than ample support in the specification and the claims as originally filed. See, for example, page 44, lines 1 - 20; and p. 41, lines 12 - 16.

**1. The Claims are Definite**

Claims 6 and 8 are rejected under 35 U.S.C. §112, second paragraph as indefinite. Claim 6 has been amended to spell out the acronym NIKS. Claim 8 has been amended to specify that the claimed composition can comprise cells from a patient. These claims have been amended to further Applicant's business interests and the prosecution of the present application in a manner consistent with the PTO's Patent Business Goals (PBG; 65 Fed. Reg. 54603 (September 8, 2000)), and not in acquiescence to the Examiner's arguments and while reserving the right to prosecute the original (or similar) claims in the future. None of the claim amendments made herein are intended to narrow the scope of any of the amended claims within the meaning of *Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co.*, 234 F.3d 558, 56 USPQ2d 1865 (Fed. Cir. 2000) or related cases. Thus, the scope of the claims has not changed due to these amendments.

**2. The Claims are Enabled**

Claims 1, 2, 5, 6, and 8 are rejected under 35 U.S.C. §112, first paragraph as non-enabled. In particular, the Examiner states that the specification fails to provide adequate guidance and evidence how to prepare a human skin equivalent having an SEC of 40-240 pf or 80-120 pf in vitro. As evidence, the Examiner refers to the disclosures of Boyce et al. and Goretsky et al. of the SEC values for cultured skin substitutes (CSS).

In rebuttal of the Examiner's arguments, the Applicants have submitted the Declaration Dr. Allen Comer, one of the inventors of the application. This Declaration establishes that skin equivalents prepared substantially as described in the application exhibit SEC readings (the difference in capacitance at 10 second intervals) in the claimed ranges prior to grafting. Thus, the Examiner's position has been rebutted by factual evidence of enablement for the claimed ranges.

**3. The Claims are Not Anticipated By Goretsky et al.**

Claims 1, 2, and 5 are rejected under 35 U.S.C. §102(b) as being anticipated by Goretsky et al., Wound Repair and Regen. 3(4):419-25 (1995). The Federal Circuit has stated the relevant analysis for anticipation as follows:

A claim is anticipated only if each and every element as set forth in the claims is found, either expressly or inherently described, in a single prior art reference."

*Verdegaal Bros. v. Union Oil Co. Of California*, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987).

The Examiner states that:

Goretsky teaches a preparation of cultured skin substitutes (CSS) by growing primary cultures of human epidermal keratinocytes and fibroblasts and inoculating these cells onto collagen-glycosaminoglycan biopolymer substrates. Goretsky records the SEC of the CSS on **postoperative** days 12, 12, 21, and 28 at 129, 200, 88 and 74 (+- deviation ) pfs. Office Action, pp. 5-6, emphasis added. As presently amended, the claims are directed to **pre-graft** human skin equivalents. Thus, the claims are not anticipated by the post-operative CSS of Goretsky.

#### **4. The Claims are Not Anticipated by Boyce et al.**

Claims 1 and 5 are rejected under 35 U.S.C. §102(b) as being anticipated by Boyce et al., J. Invest. Dermat. 107(1):82-7 (1996). The Examiner states that:

Boyce teaches preparation of CSS by culturing human epidermal fibroblasts and epidermal keratinocytes and shows SEC of the human skin substitute **after grafting** is about 40 pf.

Office Action, p. 6, emphasis added. As presently amended, the claims are directed to **pre-graft** human skin equivalents. Thus, the claims are not anticipated by the after graft CSS of Goretsky.

#### **5. The Claims are Not Obvious**

Claims 1 and 8 are rejected under 35 U.S.C. §103(a) as unpatentable over Boyce et al. in view of Suzuki et al., Transplantation 59:1236-41 (1995) and Claims 1, 3, and 4 are rejected under 35 U.S.C. §103(a) as unpatentable over Boyce et al. in view of Ponec et al., J. Invest. Dermat. 109(3):348-55 (1997). A *prima facie* case of obviousness requires the Examiner to provide a reference(s) which (a) discloses all of the elements of the claimed invention, (b) suggests or motivates one skilled in the art to combine the claimed elements to produce the claimed combination, and (c) provides a reasonable expectation of success should the claimed combination be carried out. Failure to establish any one of these three requirements precludes a finding of a *prima facie* case of obviousness and without more entitles the Applicants to allowance of the claims in issue. See, e.g., *Northern Telecom Inc. v. Datapoint Corp.*, 15 USPQ2d 1321, 1323 (Fed. Cir. 1990). Applicants respectfully submit that the cited references neither teach nor suggest each element of the claims. Thus, the Claims are not obvious.

With respect to both obviousness rejections, the Examiner again states that:

Boyce teaches preparation of CSS by culturing human epidermal fibroblasts and epidermal keratinocytes and shows SEC of the human skin substitute **after grafting** is about 40 pf.

Office Action, p. 6, emphasis added. As presently amended, the claims are directed to **pre-graft** human skin equivalents. It is respectfully submitted that neither combination of references teaches or suggests pre-graft skin equivalents with SEC reading in the claimed range. Furthermore, it is noted that Boyce actually teaches away from the claimed compositions by stating:

Therefore, skin substitutes are capable of forming a stable barrier *in vivo*, but these culture conditions do not yet support expression of this definitive phenotype of human skin *in vitro*.

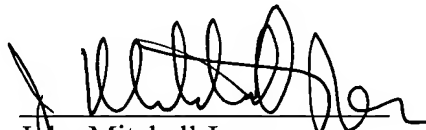
Boyce et al., p. 84, column 1.

Thus, Boyce et al. explicitly state that their culture methods cannot produce the claimed compositions. As such it is respectfully submitted that a *prima facie* case of obviousness has not been established for the present claims. Accordingly, Applicants respectfully request that the claims be passed to allowance.

## CONCLUSION

All grounds of rejection and objection of the Office Action of September 25, 2003 having been addressed, reconsideration of the application is respectfully requested. It is respectfully submitted that the invention as claimed fully meets all requirements and that the claims are worthy of allowance. Should the Examiner believe that a telephone interview would aid in the prosecution of this application, Applicant encourages the Examiner to call the undersigned collect at (608) 218-6900.

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